Application No.: 09/687,951 2 Docket No.: 146392002300

## **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-19 (Canceled)

Claim 20 (Previously Presented): A method for administering a biologically active agent, the method comprising:

injecting a formulation comprising:

- (a) an injection vehicle comprising hyaluronic acid or sodium hyaluronate dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight per volume; and
  - (b) particles comprising:
    - (i) a first component that is the biologically active agent; and
    - (ii) a second component that is a biocompatible polymeric matrix,

wherein the concentration of the particles is about 100 mg/mL to about 500 mg/mL of the formulation,

and further wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 23-gauge or smaller bore needle.

Claim 21 (Canceled)

Claim 22 (Previously Presented): An injectable formulation, comprising:

- (a) an injection vehicle comprising hyaluronic acid or sodium hyaluronate dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume; and
  - (b) particles, comprising:
    - (i) a first component that is a biologically active agent, and
    - (ii) a second component that is a biocompatible polymeric matrix,

wherein the concentration of the particles is about 100 mg/mL to about 500 mg/mL of the formulation,

and further wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the particles through a 23-gauge or smaller bore needle.

Claim 23 (Previously Presented): The injectable formulation of claim 22, wherein the physiological buffer comprises physiological saline.

Claim 24 (Canceled)

Claim 25 (Previously Presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a blocked polymer.

Claim 26 (Previously Presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises an unblocked polymer.

Claim 27 (Previously Presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises poly(lactide-co-glycolide).

Claim 28 (Previously Presented): The injectable formulation of claim 22, wherein the biologically active agent is a polypeptide.

Claim 29 (Currently Amended): The injectable formulation of claim 28, wherein the polypeptide is selected from the group consisting of a growth hormone, a cytokine; a cytokine receptor; a chimeric protein comprising a cytokine or its receptor; a tumor necrosis factor; a tumor necrosis factor receptor; a tumor necrosis factor derivative; a lipoprotein; a clotting factor; an anticlotting factor; a serum albumin; a microbial protein; a receptor for a hormone; a receptor for a growth factor; a rheumatoid factor; a neurotrophic factor; a nerve growth factor; a fibroblast growth factor; a transforming growth factor (TGF); a CD protein; an osteoinductive factor; an immunotoxin; a bone morphogenetic protein (BMP); an interferon; a colony stimulating factor (CSF); an interleukin (IL); a viral antigen; a transport protein; a homing receptor; a regulatory protein; an antibody; a portion of an antibody; a chimeric protein, a plasminogen activator; a tissue-type plasminogen activator; a urokinase; an insulin-like growth factor binding protein; a T-cell

receptor; a surface membrane protein; an HIV-1 envelope glycoprotein; a fragment of gp120; a fragment of gp160; a Fab fragment; and an immunoadhesin.

Claim 30 (Canceled)

Claim 31 (Previously Presented): The injectable formulation of claim 22, wherein the concentration of the particles in the formulation is about 1 100 mg/mL to about 300 mg/mL.

Claim 32 (Canceled)

Claim 33 (Previously Presented): The injectable formulation of claim 22, wherein the injection vehicle comprises hyaluronic acid.

Claim 34 (Previously Presented): The injectable formulation of claim 22, wherein the injection vehicle comprises sodium hyaluronate.

Claim 35 (Canceled)

Claim 36 (Previously Presented): The injectable formulation of claim 28, wherein the polypeptide is an anti-vascular endothelial growth factor Fab (anti-VEGF Fab).

Claim 37-39 (Canceled)

Claim 40 (Previously Presented): The method of claim 20, wherein the concentration of hyaluronic acid or sodium hyaluronate is about 0.01 to about 1 percent weight per volume.

Claim 41 (Previously Presented): The method of claim 40, wherein the concentration of hyaluronic acid or sodium hyaluronate is about 0.01 to about 0.8 percent weight per volume.

Claim 42 (Previously Presented): The injectable formulation of claim 22, wherein the concentration of hyaluronic acid or sodium hyaluronate is about 0.01 to about 1 percent weight per volume.

Claim 43 (Previously Presented): The injectable formulation of claim 42, wherein the concentration of hyaluronic acid or sodium hyaluronate is about 0.01 to about 0.8 percent weight per volume.

## Claim 44 (Canceled)

Claim 45 (Previously Presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a polymer selected from a biodegradable polymer, a non-biodegradable polymer, a mixture of biodegradable and non-biodegradable polymers, and a copolymer comprising biodegradable and non-biodegradable units.

Claim 46 (Previously Presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a polymer selected from blocked polymers, unblocked polymers, and mixtures of blocked and unblocked polymers.

Claim 47 (Previously Presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a polymer selected from a poly (glycolide); a poly (lactide-coglycolide); a poly (lactic acid); a poly (glycolic acid); a poly (lactic acid- co-glycolic acid); a polyanhydride; a polyorthoester; a polyetherester; a polycaprolactone; a polyesteramide; a block copolymer of polyethylene glycol and lactide; a block copolymer of polyethylene glycol and glycolide; and blends or copolymers thereof.

Claim 48 (Previously Presented): A method for making a pharmaceutical formulation, comprising:

adding an effective amount of a biologically active agent coated on, dispersed within, or coated on and dispersed within polymeric particles to an aqueous injection vehicle comprising hyaluronic acid or sodium hyaluronate at a concentration of about 0.01 to about 3% (w/v);

wherein the concentration of particles in the formulation is between about 100 and 500 mg/mL (w/v); and further wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the particles through a 23-gauge or smaller bore needle.

Claim 49 (Currently Amended): A method for administering the injectable formulation of claim 22, the method comprising[[:]] injecting the injectable formulation through a 23-gauge or smaller bore needle.

Claim 50 (Previously Presented): The injectable formulation of claim 22, wherein the biologically active agent is dispersed within, coated on, or dispersed within and coated on the particles.

Claim 51 (Previously Presented): The injectable formulation of claim 50, wherein the biologically active agent is dispersed within the particles.

Claim 52 (Previously Presented): The injectable formulation of claim 22, wherein the particles are microparticles.

Claim 53 (Previously Presented): The injectable formulation of claim 22, wherein the particles are microspheres.

Claim 54 (Previously Presented): The injectable formulation of claim 22, wherein the particles have an average diameter of between about 5 and about 200 microns.

Claim 55 (Previously Presented): The injectable formulation of claim 42, wherein the concentration of hyaluronic acid or sodium hyaluronate is between about 0.05 and about 1 percent weight per volume.

Claim 56 (Previously Presented): The injectable formulation of claim 42, wherein the concentration of hyaluronic acid or sodium hyaluronate is between about 0.05 and about 0.8 percent weight per volume.

Claim 57 (Previously Presented): The injectable formulation of claim 22, wherein the concentration of particles in the formulation is between about 125 mg/mL to about 250 mg/mL.

Claim 58 (Previously Presented): The injectable formulation of claim 22, wherein the concentration of particles in the formulation is between about 200 mg/mL to about 250 mg/mL.

Claim 59 (Previously Presented): The injectable formulation of claim 28, wherein the polypeptide is selected from the group consisting of tumor necrosis factor-alpha (TNF-alpha); tumor necrosis factor-beta (TNF-beta); tumor necrosis factor receptor-1 (TNFR-1); tumor necrosis factor receptor-2 (TNFR-2); renin; human growth hormone; bovine growth hormone; growth hormone releasing factor; parathyroid hormone; thyroid stimulating hormone; alpha-1-antitrypsin; insulin Achain; insulin B-chain; proinsulin; follicle stimulating hormone; calcitonin; luteinizing hormone; glucagon; factor VIIIC; factor IX; tissue factor; von Willebrand's factor; Protein C; atrial natriuretic factor; lung surfactant; bombesin; thrombin; hemopoietic growth factor; enkephalinase; RANTES; human macrophage inflammatory protein (MIP-1-alpha); human serum albumin; mullerianinhibiting substance; relaxin A-chain; relaxin B-chain; prorelaxin; mouse gonadotropin-associated peptide; beta-lactamase; DNase; inhibin; activin; vascular endothelial growth factor (VEGF); anti-VEGF Fab; glucagon-like peptide I (GLP-I); hepatocyte growth factor (HGF); integrin; protein A; protein D; bone-derived neurotrophic factor (BDNF); neurotrophin-3, -4, -5, and -6 (NT-3, NT-4, NT-5, NT-6); NGF-beta; platelet-derived growth factor (PDGF); aFGF; bFGF; epidermal growth factor (EGF); TGF-alpha; TGF-beta, including TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta4, and TGF-beta5; insulin-like growth factor-I (IGF-I); insulin-like growth factor-II (IGF-II); des (1-3)-IGF-I (brain IGF-I); CD-3; CD-4; CD-8; CD-19; erythropoietin; interferon-alpha; interferon-beta; interferon-gamma; M-CSF; GM-CSF; G-CSF; IL-1; IL-2; IL-3; IL-4; IL-5; IL-6; IL-7; IL-8; IL-9; IL-10; superoxide dismutase; decay accelerating factor; gp120; gp160; and addressin.

Claim 60 (Previously Presented): The method of claim 20, wherein the injection vehicle comprises hyaluronic acid.

Claim 61 (Previously Presented): The method of claim 20, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 24-gauge needle.

Claim 62 (Previously Presented): The method of claim 20, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 25-gauge needle.

Claim 63 (Previously Presented): The method of claim 20, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 26-gauge needle.

Claim 64 (Previously Presented): The method of claim 20, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 27-gauge needle.

Claim 65 (Previously Presented): The method of claim 20, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 28-gauge needle.

Claim 66 (Previously Presented): The method of claim 20, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 30-gauge needle.

## Claim 67 (Canceled)

Claim 68 (Previously Presented): The injectable formulation of claim 22, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 24-gauge needle.

Claim 69 (Previously Presented): The injectable formulation of claim 22, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 25-gauge needle.

Claim 70 (Previously Presented): The injectable formulation of claim 22, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 26-gauge needle.

Claim 71 (Previously Presented): The injectable formulation of claim 22, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 27-gauge needle.

Claim 72 (Previously Presented): The injectable formulation of claim 22, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 28-gauge needle.

Claim 73 (Previously Presented): The injectable formulation of claim 22, wherein the hyaluronic acid or sodium hyaluronate is at a concentration sufficient to inject the formulation through a 30-gauge needle.